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TITLE: Materials Research Society Symposium Proceedings. Volume 723. Molecularly Imprinted Materials - Sensors and Other Devices. Symposia Held in San Francisco, California on April 2-5, 2002

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A SELF-LOCKING TECHNIQUE WITH FAST RESPONSE AND HIGH SENSITIVITY FOR MICRO-CANTILEVER BASED SENSING OF ANALYTES

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ABSTRACT

MEMS based microcantilevers have been employed as sensors in both liquid and ambient conditions. One scheme for detection is based upon monitoring the change in microcantilever resonant frequency as a function of the adsorbed analyte concentration. However, the sensitivity is limited by the accuracy of the frequency measurements, which is a function of the *Q*-factor of the vibrating element and the measurement bandwidth. In this paper, we present a feedback scheme for self-locking amplification of the small-amplitude thermal oscillations of the microcantilever. Using this approach, we demonstrate an improvement in the *Q*-factor by two to three orders of magnitude as compared to that of the undriven microcantilever. Use of this technique eliminates the need for lock-in detection and results in improved response times for sensor applications. Experiments using the proposed feedback amplification technique show improved sensitivity for the detection of biological molecules in liquids, and for adsorbed vapors under ambient conditions.

INTRODUCTION

The field of chemical and biological sensing is increasingly turning to microelectromechanical systems (MEMS) based devices to perform rapid measurements of specific chemical species with high selectivity and sensitivity. Microcantilevers used for imaging in atomic force microscopes show a response because of interatomic forces between the surface and the cantilever tip. This phenomenon has been exploited to use the cantilever as a sensor/transducer giving birth to a new class of chemical and biological sensors [1,2,3,4]. In such sensors, the microcantilever surface is treated with a specific coating or receptor molecules. On exposure to the sample, the target molecules bind to the surface. This step can be detected by either monitoring the deflection of the cantilever (DC detection) or by measuring the change in its resonant frequency (AC detection). Various techniques such as optical beam deflection, variation in piezoresistive, capacitive or piezoelectric response are used to quantify the amount analyte bound. Microcantilever sensors developed for gas phase environments have been demonstrated to have a picogram mass resolution [5]. For many applications, especially for biological samples, sensors need to function in a liquid environment. The development of microcantilever based sensors for detection in liquid faces two drawbacks: (i) a drift in the cantilever deflection due to thermal fluctuations in the flow chamber[6] and (ii) the reduction in the quality factor (*Q*) of the microcantilever when it is immersed in liquids [7,8]. Cantilevers exhibit a measurable amplitude of vibrations due to thermal or ambient induced oscillations [9,10]. With an increasing trend towards miniaturization, manipulation and control of thermal motion of microcantilevers can result in simpler, cheaper and portable devices.

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Typical amplitude of vibration of a microcantilever with a spring constant of 0.1 N/m is approximately 0.1 nm. This amplitude is too small which limits its applicability in detection, imaging and sensing. For typical microscopy and sensing applications, such cantilevers are used with a piezoelectric bimorph, which are driven with a frequency close to the natural resonant frequency of the cantilever thus enhancing the amplitude of vibrations [9]. Recently, various methods have been attempted to control the dynamics of cantilever vibrations in an effort to improve the sensitivity of the cantilever of both imaging and sensing applications [11,12,13]. It has been shown recently that by modifying the input signal to the piezoelectric bimorph, the vibrating characteristics of the cantilever can be favorably modified. Alternatively, it has also been shown that the thermal vibrations of the cantilever can be amplified and used to drive the cantilever in a feedback mode with a resultant large increase in the Q factor of the cantilever [8]. In this paper, we utilize the self tuning amplification phenomena of the phase shifted feedback signal to demonstrate its applicability in sensing applications in gas and liquid environments. This technique improves the minimum detectable frequency shift thus improving the sensitivity of detection. By eliminating the need for external excitation of the cantilever using frequency sweep generator, fast kinetics of adsorption and binding to surfaces can also be studied.

EXPERIMENTAL METHOD

Commercially available V-shaped silicon nitride and silicon cantilevers (Thermomicroscopes) were used without any modifications for these studies. Typical dimensions of the cantilevers were, length: 100-200 μm ; width: 20-40 μm ; and thickness: 0.7-1 μm . These were mounted in a cantilever holder used for tapping mode atomic force microscopy with a built-in piezoelectric bimorph that drives the cantilever (Digital Instruments). The motion of the cantilever was detected using a laser beam reflected off the free end of the cantilever into a split-quadrant photo-diode. Figure 1 shows a schematic diagram of the experimental setup used. Briefly, The vertical difference output from the photo-diode was routed through a variable gain amplifier and phase shifter before it was applied to the piezoelectric bimorph of the cantilever holder. The vertical difference signal was analyzed in the frequency domain using an FFT spectrum analyzer.

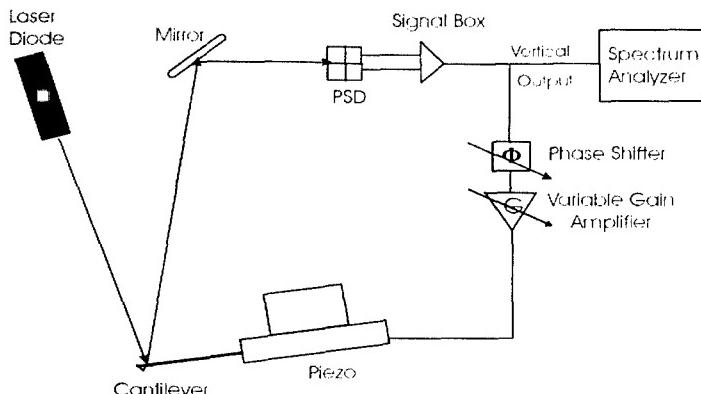


FIGURE 1. Schematic diagram of the experimental setup for measurements of cantilever resonance with a feedback loop. The laser diode, position-sensitive detector and associated electronics were housed in a commercially available head used for atomic force microscopy.

For gas phase experiments, silicon cantilevers were exposed to TNT vapors by placing a piece of solid TNT 2-3 cm below the cantilever surface. The vapor pressure of TNT near the cantilever was varied by changing the temperature of the solid piece of TNT placed in the oven. A shutter was used to control the start and end of exposure. Experiments in liquids were done in a fluid cell (Digital Instruments) with a reservoir volume of 300 μ l. The cantilever was placed in phosphate buffered saline (PBS) and allowed to equilibrate for two hours. A syringe pump (IITC Inc.) was used to pump buffer solution and the analytes through the flow cell. After equilibration 1 ml of biotin (0.2 mg/ml) was injected through a multiport injection valve (Upchurch Scientific), and approximately 2 h later 1 ml of neutravidin (0.2 mg/ml) was injected. The resonant frequency was monitored as a function of time under feedback driven conditions.

RESULTS AND DISCUSSION

Figure 2 shows the frequency response of the cantilever in air (A) and in liquid (B) to thermally induced vibrations. Typical amplitudes of cantilever due to thermal oscillations in air and water range from 0.01 to 0.1 nm (shown as solid lines in Figure 2). The fundamental resonant frequency of the cantilever is reduced due to the increased viscous drag effects in water. Secondly, and more importantly the Q factor decreases dramatically from approximately 20 in air to 1.8 in water. This is due to the hydrodynamic damping between the cantilever and the liquid environment. The amplitude of the oscillations is of the order of a few hundred microvolts. The frequency response of the feedback driven cantilever is shown in solid lines in Figure 2. The amplitude of cantilever oscillations was three orders of magnitude higher in both air and liquid. More significantly, the Q factor improved to 2975 (in air) and 20 (in water). In liquid medium detection of the fundamental frequency using a piezo bimorph by external sweeping is complicated by the appearance of multiple peaks due to excitation of acoustic waves in the reservoir. The feedback amplification technique eliminates the need for an external frequency sweep signal as it locks to the fundamental resonant frequency of the vibrating cantilever.

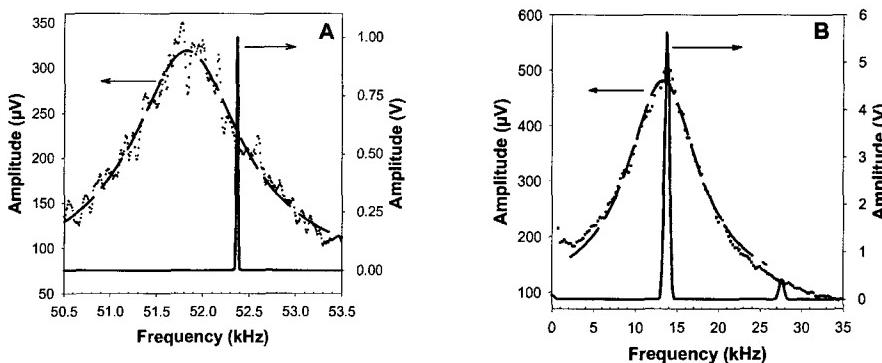


FIGURE 2. Frequency spectra for a Si_3N_4 cantilever (length = 100 μm ; spring constant, $k = 0.32$ N/m) in (A) air, and (B) water. The raw data for undriven vibrations is shown by solid circles, the Lorentzian fit is shown by the dashed lines and the phase shifted feedback driven response is shown by solid lines.

For thermally induced (undriven) vibrations the resonance peak appears as a very broad peak with full width at half maximum (FWHM) = 8.5 kHz, (Figure 2B, dashed line). The vibrations due to the phase shifted and amplified feedback drive signal in liquid exhibited a significantly sharper peak with FWHM = 0.65 kHz, as shown in Figure 2B (solid line). The amplitude was amplified by three orders of magnitude, and the Q-factor improved from 1.8 to 19. Due to the smaller FWHM, frequency measurements can be made at a smaller linewidth setting for the spectrum analyzer. This improves the minimum detectable frequency shift ($\Delta\omega$) from 15 Hz for the undriven motion to 1 Hz for the feedback driven cantilever. Similar results were also observed for rectangular, silicon cantilevers.

For detection in gas phase environments, the adsorption of TNT vapors on the cantilever surface was studied. Figure 3 shows the variation in resonant frequency of the microcantilever as a function of time when its surface was exposed to TNT vapors by opening the shutter. As increasing amounts of TNT were adsorbed on the surface of the cantilever, the increase in its effective mass resulted in a drop in the fundamental resonant frequency (ω_0). The minimum detectable shift in frequency, $\Delta\omega$, is approximately ω_0/Q . Thus, an increase in the Q factor by 2-3 orders of magnitude improves the resolution of detection significantly. Figure 3 (inset) shows that feedback driven technique allows rapid frequency shift measurements. When employing the traditional frequency sweep method to detect small shifts in resonant frequency, the resolution bandwidth of the frequency detection device needs to be reduced which increases the sweep time for each acquisition cycle. Since the feedback drive signal is always locked to the fundamental resonant frequency of the vibrating cantilever, this problem is circumvented, allowing for rapid measurements. Thus, this technique could be used for kinetic measurements of adsorption/desorption studies.

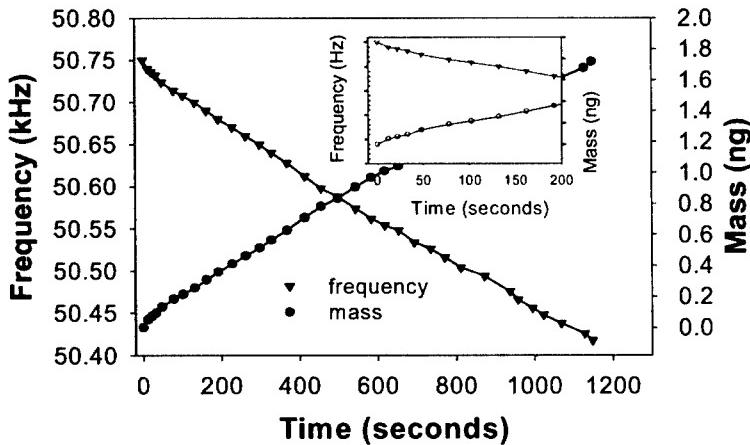


Figure 3. Variation in the resonant frequency of the feedback driven microcantilever and the adsorbed mass as a function of time during adsorption of TNT. Inset shows data for the first 200 sec.

to bind to the gold-coated side of the cantilever. The resonance frequency of the cantilever dropped as a function of biotin binding from 9.67 kHz to 9.35 kHz, as shown in Figure 3. Subsequent injection of neutravidin, which binds to the biotin on the cantilever, showed a further drop of 1.7 kHz in the fundamental resonance frequency. The sensitivity of feedback driven cantilever sensors is improved due to the higher Q factor. The minimum detectable mass (Δm_{\min}) for a cantilever is proportional to $\Delta\omega/\Delta\omega_0$. Since the minimum detectable frequency shift is markedly improved with the feedback, the sensitivity improved by an order of magnitude. By attaching specific receptors or antibodies to the surface of the cantilever, these sensors can be designed to exhibit selectivity for specific analytes.

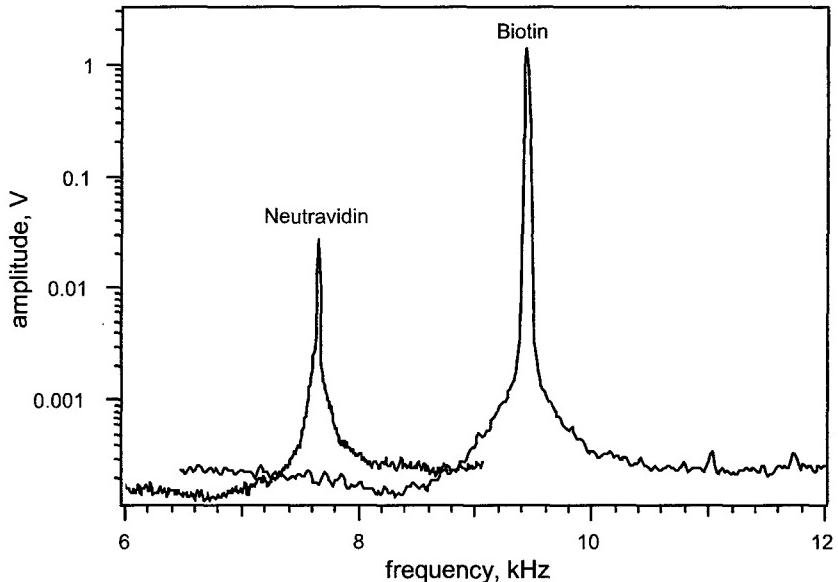


FIGURE 4. Resonant frequency shift of a feedback driven Si_3N_4 cantilever in PBS during binding with biotin and neutravidin at different times (1) 25 min., $\omega_0 = 9.656$ kHz, (2) 30 min., $\omega_0 = 9.437$ kHz, (3) 60 min., $\omega_0 = 9.434$ kHz. After two hours, neutravidin was injected and allowed to bind with the same cantilever. (4) 15 mins. after neutravidin injection, $\omega_0 = 7.648$ kHz.

CONCLUSIONS

The applicability of feedback enhanced amplification of thermal oscillations of microcantilevers for use in sensors has been demonstrated in ambient and liquid environments. The sensitivity of detection is significantly improved due to the increase in the Q factor of the cantilever. The

improvement in the resolution bandwidth for frequency shift measurements also makes this technique applicable for kinetic studies of adsorption.

ACKNOWLEDGEMENTS

This research was supported by the DOE Office of Biological and Environmental Research (OBER). Oak Ridge National Laboratory is managed by UT-Battelle, L.L.C. for the US Department of Energy under Contract No. DE-AC05-00OR22725.

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